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L1: Entry 2 of 9

File: USPT

Jul 2, 2002

DOCUMENT-IDENTIFIER: US 6413936 B1 TITLE: Glycomimetics as selectin antagonists and pharmaceuticals having antiinflammatory activity

Brief Summary Text (4):

The circulation of blood cells, for example leukocytes, neutrophils, granulocytes and monocytes, is, at the molecular level, a highly complex multistage process of which only individual steps are known (for a review see: Springer, Cell 76:301-314 (1994)). Recent research has shown that both localization of neutrophils and monocytes at foci of inflammation and lymphocyte recirculation, which is crucial in immune monitoring, respond to very similar molecular mechanisms. Thus, in acute and chronic inflammatory processes leukocytes adhere to endothelial cells and migrate to the focus of inflammation and into the secondary lymphatic organs. This process involves numerous specific signal molecules, for example interleukins, <u>leukotrienes</u> and tumor necrosis factor (TNF), G-protein coupled receptors and, in particular, tissue-specific cell adhesion molecules, which precisely control immune cell and endothelial cell recognition. The most important adhesion molecules involved in this process, designated below as receptors, include the selectins (E-, P- and L-selectins), integrins and the members of the immunoglobulin superfamily.

Brief Summary Text (6):

The tetrasaccharides sialyl-Lewis-X (SLeX) and sialyl-Lewis-A (SLeA), which occur as substructures of glycosphingolipids and glycoproteins on cell membranes, can function as ligands for all three selectin receptors. A series of glycoproteins, mucins and glycolipids are known to be suitable endogenous ligands for the selecting. These include: Mucosal Vascular Addressin MadCAM-1 (Berg et al., Nature 366:695 (1993)) and Sialomucin CD34 (Baumhuter et al., Science 262:436 (1993)) for L-selectin: O-linked polylactosamine-sialomucin <u>PSGL-1</u> on human neutrophils for P-selectin (Moore et al., J.Biol.Chem. 269:23318 (1994); and N-linked sialoglycoproteins of the ESL-1 type for E-selectin (Vestweber et al., Cell Biol. 121:449 (1993)).

Brief Summary Text (87):

This receptor-mediated interaction of leukocytes and endothelial cells is regarded as an initial sign of the inflammatory process. In addition to the adhesion molecules already physiologically expressed, under the action of inflammatory mediators (<u>leukotrienes</u>, platelet activating factor) and cytokines (TNF-alpha, interleukins), a temporally graded, massive expression of adhesion molecules takes place on the cells. They are at present divided into three groups: the immunoglobulin gene superfamily, the integrins, and the selecting. Whereas adhesion takes place between molecules of the Ig gene superfamily and the protein-protein bonds, lectin-carbohydrate bonds are predominant in the interaction of selectins (Springer, Nature 346:425 (1990); Hughes, Scrips Magazine 6:30 (1993); Springer, Cell 76:301 (1994)).

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L1: Entry 4 of 9

File: USPT

May 1, 2001

DOCUMENT-IDENTIFIER: US 6225071 B1 TITLE: Methods of screening for compounds which mimic galectin-1

Brief Summary Text (7):

Some of the important factors that mediate endothelial-neutrophil adhesion to initiate the inflammatory response are: bacterial products (e.g., endotoxin), complement fragments (e.g., C5a), chemotactic peptides, <u>leukotriene</u> B.sub.4 (LTB.sub.4), platelet activating factor (PAF), transferrin, and cytokines (e.g., IL-1 and TNF). These mediators stimulate activation of neutrophils and/or endothelial cells leading to expression of important adhesion molecules, such as integrins and selectins that mediate neutrophil binding. The adhesion of neutrophil to activated endothelium leads to neutrophil activation. Activated neutrophils have enhanced adhesion properties and the cells are highly migratory. The cells are also chemotactic and phagocytic. It is largely through their phagocytic activity that neutrophils promote clearance of infectious organisms.

Brief Summary Text (14):

In addition, as noted above, it is now known that the neutrophil adhesion to activated endothelium is a prerequisite for the inflammatory response. Proteins expressed by activated endothelium which are critical for neutrophil adhesion are selecting, such as P-selectin and E-selectin, and the immunoglobulin (Ig) superfamily members, such as CD54 (intercellular adhesion molecule-1 or ICAM-1). Neutrophils also express surface adhesion molecules, such as the .beta.2 integrin LFA-1 (CD11a,b,c/CD18), which binds to ICAM-1, and L-selectin, which binds P-Selectin glycoprotein ligand-1 (PSGL-1) on already adherent neutrophils and heparan sulfate-related molecules on activated endothelial cells. However, of paramount importance to the initial steps in inflammation, is the adhesion of neutrophils to selecting on endothelial cells. The general roles of adhesion molecules in inflammation are discussed in "The Sensation and Regulation of Interactions within the Extracellular Environment: The Cell Biology of Lymphocyte Adhesion Receptors" (1990) by T. A. Springer, in the Annual Review of Cell Biology, Vol. 6:359-402.

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Search Results -	, <u></u>
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LEUKOTRIENES.DWPI,EPAB,JPAB,USPT,PGPB.	3478
PSGL\$	0
PSGL.DWPI,EPAB,JPAB,USPT,PGPB.	83
"PSGLB1/MIGG.SUB.2B".DWPI,EPAB,JPAB,USPT,PGPB.	1
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PSGLSPSLCP.DWPI,EPAB,JPAB,USPT,PGPB.	2
PSGLU.DWPI,EPAB,JPAB,USPT,PGPB.	1
PSGL1.DWPI,EPAB,JPAB,USPT,PGPB.	1
"PSGL1/MIGG.SUB.2B".DWPI,EPAB,JPAB,USPT,PGPB.	1
PSGL2.DWPI,EPAB,JPAB,USPT,PGPB.	13
(PSGL\$ AND LEUKOTRIENE).USPT,PGPB,JPAB,EPAB,DWPI.	9

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DB=USPT,PGPB,	JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ		
<u>L1</u>	psgl\$ and leukotriene	9	<u>L1</u>

END OF SEARCH HISTORY

Set Items Description ----_____ ? s psql? and (leukotriene or ltc4) 973 PSGL? 49135 LEUKOTRIENE 4554 LTC4 1 PSGL? AND (LEUKOTRIENE OR LTC4) S1 ? t s1/3/all (Item 1 from file: 399) 1/3/1 DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 132203144 CA: 132(16)203144s PATENT Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders INVENTOR (AUTHOR) : Nyce, Jonathan W. LOCATION: USA ASSIGNEE: East Carolina University PATENT: PCT International ; WO 200009525 A2 DATE: 20000224 APPLICATION: WO 99US17712 (19990803) *US 95212 (19980803) PAGES: 1343 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-000/A DESIGNATED COUNTRIES: AU; CA; CN; MX; RU; US DESIGNATED REGIONAL: AT; BE ; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE ? t s1/kwic/all >>>KWIC option is not available in file(s): 399 ? s (thrombosis or thrombotic) and (ltc4 or leukotriene(w)4) 201240 THROMBOSIS 37469 THROMBOTIC 4554 LTC4 49135 LEUKOTRIENE 5466523 4 33 LEUKOTRIENE(W)4 10 (THROMBOSIS OR THROMBOTIC) AND (LTC4 OR LEUKOTRIENE(W)4) S2 ? rd s2 ... completed examining records 8 RD S2 (unique items) S3 ? t s3/3/all (Item 1 from file: 5) 3/3/1 DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07396805 BIOSIS NO.: 000091012415 TRANSCELLULAR BIOSYNTHESIS OF SULFIDOPEPTIDE LEUKOTRIENES DURING RECEPTOR-MEDIATED STIMULATION OF HUMAN NEUTROPHIL-PLATELET MIXTURES AUTHOR: MACLOUF J; MURPHY R C; HENSON P M AUTHOR ADDRESS: NATIONAL JEWISH CENTER IMMUNOLOGY RESPIRATORY MEDICINE, 1400 JACKSON ST., DENVER, COLO. 80206. JOURNAL: BLOOD 76 (9). 1990. 1838-1844. 1990 FULL JOURNAL NAME: Blood CODEN: BLOOA RECORD TYPE: Abstract LANGUAGE: ENGLISH (Item 2 from file: 5) 3/3/2 5:Biosis Previews(R) DIALOG(R)File (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 000088092372 06782935 TRANSCELLULAR SULFIDOPEPTIDE LEUKOTRIENE BIOSYNTHETIC CAPACITY OF VASCULAR CELLS

SetItemsDescriptionS11PSGL? AND (LEUKOTRIENE OR LTC4) 10 (THROMBOSIS OR THROMBOTIC) AND (LTC4 OR LEUKOTRIENE(W)4) 8 RD S2 (unique items) 22070 (THROMBOSIS OR THROMBOTIC) AND (ISCHEM? OR REPERFUSION OR -S2 S3 S4 RESTENOSIS) S5 142 (REPERFUSION OR ISCHEM? OR RESTENOSIS) AND (LTC4 OR LEUKOT-RIENE(W)4)41 S5 AND (MYOCARDIAL OR INFARCTION) S6 S7 33 RD S6 (unique items) ? s s5 and psgl? 142 S5 973 PSGL? S8 0 S5 AND PSGL? ? s s5 and p(w)selectin 142 S5 4056540 P 28893 SELECTIN 10871 P(W)SELECTIN S9 0 S5 AND P(W)SELECTIN

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AUTHOR: MACLOUF J; MURPHY R C; HENSON P M AUTHOR ADDRESS: DEP. PHARMACOL. C236 , UNIV. COLO. HEALTH SCI. CENT., 4200 EAST 9TH AVENUE, DENVER, COLO. 80262. JOURNAL: BLOOD 74 (2). 1989. 703-707. 1989 FULL JOURNAL NAME: Blood CODEN: BLOOA RECORD TYPE: Abstract LANGUAGE: ENGLISH 3/3/3 (Item 3 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 05170270 BIOSIS NO.: 000082010891 LEUKOTRIENES C-4 AND D-4 STIMULATE HUMAN ENDOTHELIAL CELLS TO SYNTHESIZE PLATELET-ACTIVATING FACTOR AND BIND NEUTROPHILS AUTHOR: MCINTYRE T M; ZIMMERMAN G A; PRESCOTT S M AUTHOR ADDRESS: NORA ECCLES HARRISON CARDIOVASCULAR RES. TRAINING INST., SALT LAKE CITY, UTAH 84112. JOURNAL: PROC NATL ACAD SCI U S A 83 (7). 1986. 2204-2208. 1986 FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America CODEN: PNASA RECORD TYPE: Abstract LANGUAGE: ENGLISH 3/3/4 (Item 1 from file: 155) DIALOG(R) File 155: MEDLINE(R) 96301977 PMID: 8686958 08930241 Arachidonic acid metabolites in acute myocardial infarction. Takase B; Maruyama T; Kurita A; Uehata A; Nishioka T; Mizuno K; Nakamura H; Katsura K; Kanda Y 1st Department of Internal Medicine, National Defense Medical College, Saitama, Japan. Angiology (UNITED STATES) Jul 1996, 47 (7) p649-61, ISSN 0003-3197 Journal Code: 0203706 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 2 from file: 155) 3/3/5 DIALOG(R) File 155: MEDLINE(R) 95322447 PMID: 7599181 08564646 metabolism in the human mast cell line HMC-1: Arachidonic acid 5-lipoxygenase gene expression and biosynthesis of thromboxane. Macchia L; Hamberg M; Kumlin M; Butterfield J H; Haeggstrom J Z Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden. Biochimica et biophysica acta (NETHERLANDS) Jun 27 1995, 1257 (1) p58-74, ISSN 0006-3002 Journal Code: 0217513 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed

3/3/6 (Item 3 from file: 155) DIALOG(R)File 155:MEDLINE(R) 08020785 94167673 PMID: 8122190 Intravascular cysteinyl-leukotriene formation by clotting whole human blood. Evidence from clamped umbilical vein segments and thrombus specimens. Weide I: Winking M: Simmet T

Weide I; Winking M; Simmet T Department of Pharmacology and Toxicology, Ruhr University, Bochum, Germany.

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? t s3/3/all (Item 1 from file: 5) 3/3/1 DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07396805 BIOSIS NO.: 000091012415 TRANSCELLULAR BIOSYNTHESIS OF SULFIDOPEPTIDE LEUKOTRIENES DURING RECEPTOR-MEDIATED STIMULATION OF HUMAN NEUTROPHIL-PLATELET MIXTURES AUTHOR: MACLOUF J; MURPHY R C; HENSON P M AUTHOR ADDRESS: NATIONAL JEWISH CENTER IMMUNOLOGY RESPIRATORY MEDICINE, 1400 JACKSON ST., DENVER, COLO. 80206. JOURNAL: BLOOD 76 (9). 1990. 1838-1844. 1990 FULL JOURNAL NAME: Blood CODEN: BLOOA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 3/3/2 (Item 2 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06782935 BIOSIS NO.: 000088092372 TRANSCELLULAR SULFIDOPEPTIDE LEUKOTRIENE BIOSYNTHETIC CAPACITY OF VASCULAR CELLS AUTHOR: MACLOUF J; MURPHY R C; HENSON P M AUTHOR ADDRESS: DEP. PHARMACOL. C236 , UNIV. COLO. HEALTH SCI. CENT., 4200 EAST 9TH AVENUE, DENVER, COLO. 80262. JOURNAL: BLOOD 74 (2). 1989. 703-707. 1989 FULL JOURNAL NAME: Blood CODEN: BLOOA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 3/3/3 (Item 3 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 05170270 BIOSIS NO.: 000082010891 LEUKOTRIENES C-4 AND D-4 STIMULATE HUMAN ENDOTHELIAL CELLS TO SYNTHESIZE PLATELET-ACTIVATING FACTOR AND BIND NEUTROPHILS AUTHOR: MCINTYRE T M; ZIMMERMAN G A; PRESCOTT S M AUTHOR ADDRESS: NORA ECCLES HARRISON CARDIOVASCULAR RES. TRAINING INST., SALT LAKE CITY, UTAH 84112. JOURNAL: PROC NATL ACAD SCI U S A 83 (7). 1986. 2204-2208. 1986 FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America CODEN: PNASA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 3/3/4 (Item 1 from file: 155) DIALOG(R) File 155: MEDLINE(R) PMID: 8686958 08930241 96301977 Arachidonic acid metabolites in acute myocardial infarction. Takase B; Maruyama T; Kurita A; Uehata A; Nishioka T; Mizuno K; Nakamura H; Katsura K; Kanda Y 1st Department of Internal Medicine, National Defense Medical College, Saitama, Japan. Angiology (UNITED STATES) Jul 1996, 47 (7) p649-61, ISSN 0003-3197

Journal Code: 0203706 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 2 from file: 155) 3/3/5 DIALOG(R) File 155: MEDLINE(R) 08564646 95322447 PMID: 7599181 Arachidonic acid metabolism in the human mast cell line HMC-1: 5-lipoxygenase gene expression and biosynthesis of thromboxane. Macchia L; Hamberg M; Kumlin M; Butterfield J H; Haeggstrom J Z Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden. Biochimica et biophysica acta (NETHERLANDS) Jun 27 1995, 1257 (1) p58-74, ISSN 0006-3002 Journal Code: 0217513 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 3/3/6 (Item 3 from file: 155) DIALOG(R) File 155: MEDLINE(R) 08020785 94167673 PMID: 8122190 Intravascular cysteinyl-leukotriene formation by clotting whole human blood. Evidence from clamped umbilical vein segments and thrombus specimens. Weide I; Winking M; Simmet T Department of Pharmacology and Toxicology, Ruhr University, Bochum, Germany. Thrombosis research (UNITED STATES) Oct 1 1993, 72 (1) p83-90, ISSN 0049-3848 Journal Code: 0326377 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 4 from file: 155) 3/3/7 DIALOG(R) File 155: MEDLINE(R) PMID: 3035280 05475927 87227318 of leukotrienes B4, D4 rat mesenteric Effects C4, and on microcirculation. Michelassi F; Shahinian H K; Ferguson M K Journal of surgical research (UNITED STATES) May 1987, 42 (5)p475-82, ISSN 0022-4804 Journal Code: 0376340 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 5 from file: 155) 3/3/8 DIALOG(R)File 155:MEDLINE(R) 05129677 86177572 PMID: 3457383 Leukotrienes C4 and D4 stimulate human endothelial cells to synthesize platelet-activating factor and bind neutrophils. McIntyre T M; Zimmerman G A; Prescott S M

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Apr 1986, 83 (7) p2204-8, ISSN 0027-8424 Journal Code: 7505876 Contract/Grant No.: HL00696; HL; NHLBI; R01 HL34127-01; HL; NHLBI; R01 HL35828-01; HL; NHLBI Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed ? s (thrombosis or thrombotic) and (ischem? or reperfusion or restenosis) 201240 THROMBOSIS 37469 THROMBOTIC 496889 ISCHEM? 104586 REPERFUSION 28801 RESTENOSIS S4 22070 (THROMBOSIS OR THROMBOTIC) AND (ISCHEM? OR REPERFUSION OR RESTENOSIS) ? s (reperfusion or ischem? or restenosis) and (ltc4 or leukotriene(w)4) 104586 REPERFUSION 496889 ISCHEM? 28801 RESTENOSIS 4554 LTC4 49135 LEUKOTRIENE 5466523 4 33 LEUKOTRIENE(W)4 **S**5 142 (REPERFUSION OR ISCHEM? OR RESTENOSIS) AND (LTC4 OR LEUKOTRIENE(W)4) ? s s5 and (myocardial or infarction) 142 S5 503646 MYOCARDIAL 362953 INFARCTION 41 S5 AND (MYOCARDIAL OR INFARCTION) S6 ? rd s6 ... completed examining records S7 33 RD S6 (unique items) ? t s7/3/all (Item 1 from file: 5) 7/3/1 DIALOG(R) File 5: Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 200100018477 12811328 Aspirin and asthma. AUTHOR: Babu K Suresh(a); Salvi Sundeep S AUTHOR ADDRESS: (a)University Medicine, Southampton General Hospital, Level D, Centre Block, Southampton, SO16 6YD: ksb@soton.ac.uk**UK JOURNAL: Chest 118 (5):p1470-1476 November, 2000 MEDIUM: print ISSN: 0012-3692 DOCUMENT TYPE: Literature Review RECORD TYPE: Abstract LANGUAGE: English SUMMARY LANGUAGE: English 7/3/2 (Item 2 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07946333 BIOSIS NO.: 000093025431 INTRACORONARY C5A INDUCES MYOCARDIAL ISCHEMIA BY MECHANISMS INDEPENDENT OF THE NEUTROPHIL LEUKOCYTE FILTERS DESENSITIZE THE MYOCARDIUM TO C-5A AUTHOR: ENGLER R L; ROTH D M; DEL BALZO U; ITO B R

AUTHOR ADDRESS: RES. SERV., VETERANS ADM. MED. CENT., 3350 LA JOLLA VILLAGE DR., SAN DIEGO, CALIF. 92161, USA. JOURNAL: FASEB (FED AM SOC EXP BIOL) J 5 (14). 1991. 2983-2991. 1991 FULL JOURNAL NAME: FASEB (Federation of American Societies for Experimental Biology) Journal CODEN: FAJOE RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/3 (Item 3 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07748050 BIOSIS NO.: 000092061771 THE EFFECT OF LEUKOTRIENE LTC-4 ON THE CORONARY VASCULAR BED AND MYOCARDIAL CONTRACTILITY AUTHOR: MOIBENKO A A; KOLCHIN YU N; BULAKH V N; SOROCHINSKII A E AUTHOR ADDRESS: DEP. EXP. CARDIOL., A.A. BOGOMOLETS INST. PHYSIOL., ACAD. SCI. UKR. SSR, KIEV, USSR. JOURNAL: BYULL EKSP BIOL MED 111 (2). 1991. 120-123. 1991 FULL JOURNAL NAME: Byulleten' Eksperimental'noi Biologii i Meditsiny CODEN: BEBMA RECORD TYPE: Abstract LANGUAGE: RUSSIAN 7/3/4 (Item 4 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07725005 BIOSIS NO.: 000092049636 INTRACAROTID INFUSION OF LEUKOTRIENE C-4 SELECTIVELY INCREASES BLOOD-BRAIN BARRIER PERMEABILITY AFTER FOCAL ISCHEMIA IN RATS AUTHOR: BABA T; BLACK K L; IKEZAKI K; CHEN K; BECKER D P AUTHOR ADDRESS: DIV. NEUROSURGERY, 74-140 CHS, UCLA MED. CENT., LOS ANGELES, CALIF. 90024. JOURNAL: J CEREB BLOOD FLOW METAB 11 (4). 1991. 638-643. 1991 FULL JOURNAL NAME: Journal of Cerebral Blood Flow and Metabolism CODEN: JCBMD **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/5 (Item 5 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 07059785 BIOSIS NO.: 000089129889 RESPONSES OF PLASMA EICOSANOIDS AND HEMODYNAMICS TO MYOCARDIAL ISCHEMIA AND THE SALUTARY EFFECT OF CALCIUM ENTRY BLOCKER AUTHOR: TAKASE B AUTHOR ADDRESS: DEP. BIOCHEM., NIPPON MED. SCH., 1-1-5 SENDAGI, BUNKYO-KU, TOKYO 113, JAPAN. JOURNAL: J NIPPON MED SCH 57 (1). 1990. 42-54. 1990 FULL JOURNAL NAME: Journal of Nippon Medical School CODEN: NIDZA RECORD TYPE: Abstract LANGUAGE: JAPANESE (Item 6 from file: 5) 7/3/6

DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv.

BIOSIS NO.: 000089101451 07009568 THROMBOXANE A-2 AND PEPTIDOLEUKOTRIENES CONTRIBUTE TO THE MYOCARDIAL ISCHEMIA AND CONTRACTILE DYSFUNCTION IN RESPONSE TO INTRACORONARY INFUSION OF COMPLEMENT C5A IN PIGS AUTHOR: ITO B R; ROTH D M; ENGLER R L AUTHOR ADDRESS: RES. SERV., CARDIOL. DIV. 151, VETERANS ADM., MED. CENT., 3350 LA JOLLA VILLAGE DRIVE, SAN DIEGO, CALIF. 92161. JOURNAL: CIRC RES 66 (3). 1990. 596-607. 1990 FULL JOURNAL NAME: Circulation Research CODEN: CIRUA RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/7 (Item 7 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06723393 BIOSIS NO.: 000088032819 PHARMACOLOGIC PROFILE OF LIPOXIN A-5 AND B-5 NEW BIOLOGICALLY ACTIVE EICOSANOIDS AUTHOR: STAHL G L; TSAO P; LEFER A M; RAMPHAL J Y; NICOLAOU K C AUTHOR ADDRESS: DEP. PHYSIOL., JEFFERSON MED. COLL., 1020 LOCUST STREET, PHILADELPHIA, PA. 19107. JOURNAL: EUR J PHARMACOL 163 (1). 1989. 55-60. 1989 FULL JOURNAL NAME: European Journal of Pharmacology CODEN: EJPHA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/8 (Item 8 from file: 5) DIALOG(R) File 5: Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 000087085571 06643398 EFFECTS OF A NEW THROMBOXANE A-2-ANTAGONIST ONO-3708 AND A NEW LEUKOTRIENE-ANTAGONIST ONO-1078 ON THROMBOXANE A-2 ANALOGUE LEUKOTRIENE C-4 AND D-4-INDUCED REGIONAL MYOCARDIAL BLOOD FLOW REDUCTION AUTHOR: TORII T; TOKI Y; HIEDA N; ITO Y; OKUMURA K; HASHIMOTO H; ITO T; OGAWA K; SATAKE T AUTHOR ADDRESS: THE 2ND DEP. INTERNAL MED., NAGOYA UNIV. SCH. MED., 65 TSURUMA-CHO, SHOWA-KU, NAGOYA 466, JAPAN. JOURNAL: HEART VESSELS 4 (2). 1988. 104-111. 1988 FULL JOURNAL NAME: Heart and Vessels CODEN: HEVEE RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/9 (Item 9 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06632882 BIOSIS NO.: 000087075044 EFFECT OF INHALED LEUKOTRIENE C-4 ON CARDIOPULMONARY FUNCTION AUTHOR: ALBAZZAZ M K; PATEL K R; SHAKIR S; DARGIE H J; REID J M AUTHOR ADDRESS: DEP. RESPIR. MED., WESTERN INFIRMARY, GLASGOW G11 6NT, SCOTLAND. JOURNAL: AM REV RESPIR DIS 139 (1). 1989. 188-193. 1989 FULL JOURNAL NAME: American Review of Respiratory Disease CODEN: ARDSB RECORD TYPE: Abstract

LANGUAGE: ENGLISH

7/3/10 (Item 10 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06282879 BIOSIS NO.: 000086117062 EFFICACY OF A COMBINATION THROMBOXANE RECEPTOR ANTAGONIST AND LIPOXYGENASE INHIBITOR IN TRAUMATIC SHOCK AUTHOR: LEVITT M A; STAHL G; LEFER A M AUTHOR ADDRESS: DEP. PHYSIOL., JEFFERSON MED. COLL., THOMAS JEFFERSON UNIV., 1020 LOCUST ST., PHILADELPHIA, PA. 19107, U.S.A. JOURNAL: RESUSCITATION 16 (3). 1988. 211-220. 1988 FULL JOURNAL NAME: Resuscitation CODEN: RSUSB RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/11 (Item 11 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06206742 BIOSIS NO.: 000086040924 THE EFFECTS OF LIPOXYGENASE INHIBITOR AND PEPTIDOLEUKOTRIENE ANTAGONIST ON MYOCARDIAL INJURY IN A CANINE CORONARY OCCLUSION-REPERFUSION MODEL AUTHOR: TOKI Y; HIEDA N; TORII T; HASHIMOTO H; ITO T; OGAWA K; SATAKE T AUTHOR ADDRESS: 2ND DEP. INTERN. MED., NAGOYA UNIV. SCH. MED., 65 TSURUMA-CHO, SHOWA-KU, NAGOYA 466, JPN. JOURNAL: PROSTAGLANDINS 35 (4). 1988. 555-572. 1988 FULL JOURNAL NAME: Prostaglandins CODEN: PRGLB **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/12 (Item 12 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06071598 BIOSIS NO.: 000085034747 PAF-ACETHER INDUCED CARDIAC DYSFUNCTION IN THE ISOLATED PERFUSED GUINEA-PIG HEART AUTHOR: STAHL G L; LEFER D J; LEFER A M AUTHOR ADDRESS: DEP. PHYSIOL., JEFFERSON MED. COLL., THOMAS JEFFERSON UNIV., 1020 LOCUST ST., PHILADELPHIA, PA. 19107, USA. JOURNAL: NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL 336 (4). 1987. 459-463. 1987 FULL JOURNAL NAME: Naunyn-Schmiedeberg'S Archives of Pharmacology CODEN: NSAPC RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/13 (Item 13 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 06071558 BIOSIS NO.: 000085034707 MECHANISMS OF PLATELET-ACTIVATING FACTOR-INDUCED CARDIAC DEPRESSION IN THE ISOLATED PERFUSED RAT HEART AUTHOR: STAHL G L; LEFER A M AUTHOR ADDRESS: DEP. PHYSIOL., JEFFERSON MED. COLL., 1020 LOCUST ST.,

PHILADELPHIA, PA. 19107. JOURNAL: CIRC SHOCK 23 (3). 1987. 165-178. 1987 FULL JOURNAL NAME: Circulatory Shock CODEN: CRSHA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/14 (Item 14 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 05736208 BIOSIS NO.: 000084084614 LEUKOTRIENE C-4-INDUCED AND LEUKOTRIENE D-4-INDUCED DIFFUSE PERIPHERAL CONSTRICTION OF SWINE CORONARY ARTERY ACCOMPANIED BY ST ELEVATION ON THE ELECTROCARDIOGRAM ANGIOGRAPHIC ANALYSIS AUTHOR: TOMOIKE H; EGASHIRA K; YAMADA A; HAYASHI Y; NAKAMURA M AUTHOR ADDRESS: RES. INST. ANGIOCARDIOL. CARDIOVASC. CLINIC, FAC. MED., KYUSHU UNIV., 3-1-1 MAIDASHI, HIGASHI-KU, FUKUOKA 812, JPN. JOURNAL: CIRCULATION 76 (2). 1987. 480-487. 1987 FULL JOURNAL NAME: Circulation CODEN: CIRCA RECORD TYPE: Abstract LANGUAGE: ENGLISH 7/3/15 (Item 15 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 000084043530 05695125 HETEROGENEITY OF VASCULAR SMOOTH MUSCLE RESPONSIVENESS TO LIPID VASOACTIVE MEDIATORS AUTHOR: STAHL G L; LEFER A M AUTHOR ADDRESS: DEP. PHYSIOL., JEFFERSON MED. COLL., THOMAS JEFFERSON UNIV., 1020 LOCUST ST., PHILADELPHIA, PA. 19107, USA. JOURNAL: BLOOD VESSELS 24 (1-2). 1987. 24-30. 1987 FULL JOURNAL NAME: Blood Vessels CODEN: BLVSA **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/16 (Item 16 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 05662889 BIOSIS NO.: 000084011294 REV-5901 AN ORALLY EFFECTIVE PEPTIDOLEUKOTRIENE ANTAGONIST DETAILED BIOCHEMICAL-PHARMACOLOGICAL PROFILE AUTHOR: VAN INWEGEN R G; KHANDWALA A; GORDON R; SONNINO P; COUTTS S; JOLLY S AUTHOR ADDRESS: RORER CENT. RES., BUILD. NO. 2, 805 BUSINESS CENT. DRIVE, HORSHAM, PA. 19044. JOURNAL: J PHARMACOL EXP THER 241 (1). 1987. 117-124. 1987 FULL JOURNAL NAME: Journal of Pharmacology and Experimental Therapeutics CODEN: JPETA **RECORD TYPE:** Abstract LANGUAGE: ENGLISH 7/3/17 (Item 17 from file: 5) DIALOG(R)File 5:Biosis Previews(R)

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BIOSIS NO.: 000082114786 05274161 EFFECTS OF NIFEDIPINE AND INDOMETHACIN ON LEUKOTRIENE C-4 AND LEUKOTRIENE D-4-INDUCED CORONARY CONSTRICTION AT NORMAL AND REDUCED CORONARY PERFUSION IN DOGS AUTHOR: ERTL G; FIEDLER V B; BAUER B; SCHWARZENBERGER P; KOCHSIEK K AUTHOR ADDRESS: MED. KLINIK, UNIV. WUEZBURG, JOSEF-SCHNEIDER-STR. 2, D-8700 WUERZBURG, W. GERMANY. JOURNAL: J CARDIOVASC PHARMACOL 8 (5). 1986. 1078-1085. 1986 FULL JOURNAL NAME: Journal of Cardiovascular Pharmacology CODEN: JCPCD **RECORD TYPE: Abstract** LANGUAGE: ENGLISH 7/3/18 (Item 18 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 000030026966 04833842 INHIBITION OF ARACHIDONATE METABOLISM IN MYOCARDIAL ISCHEMIA AUTHOR: MULLANE K AUTHOR ADDRESS: DEP. PHARMACOLOGY, NEW YORK MED. COLLEGE, VALHALLA, N.Y., USA. JOURNAL: 6TH MEETING OF THE INTERNATIONAL SOCIETY FOR HEART RESEARCH (EUROPEAN SECTION), STOCKHOLM, SWEDEN, SEPT. 8-11, 1985. J MOL CELL CARDIOL 17 (SUPPL. 3). 1985. NO PAGINATION. 1985 CODEN: JMCDA DOCUMENT TYPE: Meeting **RECORD TYPE:** Citation LANGUAGE: ENGLISH 7/3/19 (Item 1 from file: 155) DIALOG(R) File 155: MEDLINE(R) 09763235 98188114 PMID: 9529265 Stem cell factor in mast cells and increased mast cell density in idiopathic and **ischemic** cardiomyopathy. Patella V; Marino I; Arbustini E; Lamparter-Schummert B; Verga L; Adt M; Marone G Division of Clinical Immunology and Allergy, University of Naples Federico II, School of Medicine, Napoli, Italy. Circulation (UNITED STATES) Mar 17 1998, 97 p971-8, ISSN (10) 0009-7322 Journal Code: 0147763 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/20 (Item 2 from file: 155) DIALOG(R) File 155: MEDLINE(R) 09244641 97133714 PMID: 8979109 Consequences of transcellular biosynthesis of leukotriene C4 on organ function. Maclouf J; Sala A; Rossoni G; Berti F; Muller-Peddinghaus R; Folco G U 348 INSERM, I.F.R. Circulation-Lariboisiere, Hopital Lariboisiere, Paris, France. Haemostasis (SWITZERLAND) Oct 1996, 26 Suppl 4 p28-36, ISSN 0301-0147 Journal Code: 0371574 Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH

Main Citation Owner: NLM Record type: Completed 7/3/21 (Item 3 from file: 155) DIALOG(R)File 155:MEDLINE(R) 08891628 96245818 PMID: 8655285 Immunological characterization and functional importance of human heart mast cells. Marone G; de Crescenzo G; Adt M; Patella V; Arbustini E; Genovese A Department of Medicine, University of Naples, Italy. Immunopharmacology (NETHERLANDS) Nov 1995, 31 (1)ISSN p1-18, Journal Code: 7902474 0162-3109 Document type: Journal Article; Review; Review, Academic Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/22 (Item 4 from file: 155) DIALOG(R) File 155: MEDLINE(R) 08781837 96147870 PMID: 8556938 Effects of selenium and vitamin E on arachidonic acid metabolism in experimental myocardial ischaemia] Liu W; Li G; Zhang X Institute of Preclinical Sciences Norman Bethune University of Medical Sciences, Changchun. Zhonghua yu fang yi xue za zhi Chinese journal of preventive medicine (p279-82, ISSN 0253-9624 CHINA) 1995, 29 (5) Journal Code: Sep 7904962 Document type: Journal Article ; English Abstract Languages: CHINESE Main Citation Owner: NLM Record type: Completed 7/3/23 (Item 5 from file: 155) DIALOG(R) File 155: MEDLINE(R) 08620273 95377665 PMID: 7649495 Reduction of reperfusion injury of human myocardium by allopurinol: a clinical study. Gimpel J A; Lahpor J R; van der Molen A J; Damen J; Hitchcock J F of Clinical Chemistry, Academic Hospital, Utrecht, Department The Netherlands. Free radical biology & medicine (UNITED STATES) Aug 1995, (2) 19 p251-5, ISSN 0891-5849 Journal Code: 8709159 Document type: Clinical Trial; Journal Article; Randomized Controlled Trial Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 6 from file: 155) 7/3/24 DIALOG(R) File 155: MEDLINE(R) PMID: 7536502 08479160 95235343 Human heart mast cells: a definitive case of mast cell heterogeneity. Patella V; de Crescenzo G; Ciccarelli A; Marino I; Adt M; Marone G Division of Clinical Immunology and Allergy, University of Naples Federico II, Italy.

International archives of allergy and immunology (SWITZERLAND) Apr 1995 106 (4) p386-93, ISSN 1018-2438 Journal Code: 9211652 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/25 (Item 7 from file: 155) DIALOG(R)File 155:MEDLINE(R) 07656099 93197195 PMID: 1294940 Vasoactive eicosanoids in the rat heart: clues to a contributory role of cardiac thromboxane to post-ischaemic hyperaemia. Giannessi D; Lazzerini G; Sicari R; DeCaterina R CNR, Institute of Clinical Physiology, Pisa, Italy. Pharmacological research the official journal of the Italian : Pharmacological Society (ENGLAND) Dec 1992, 26 (4) p341-56, ISSN 1043-6618 Journal Code: 8907422 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 8 from file: 155) 7/3/26 DIALOG(R) File 155: MEDLINE(R) 07155855 92090560 PMID: 1661246 Intracoronary C5a induces myocardial ischemia by mechanisms independent of the neutrophil: leukocyte filters desensitize the myocardium to C5a. Engler R L; Roth D M; del Balzo U; Ito B R Department of Medicine and Pathology, Veterans Administration Medical Center, San Diego, California 92161. FASEB journal : official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Nov 1991, 5 (14) p2983-91, ISSN 0892-6638 Journal Code: 8804484 Contract/Grant No.: HL17682-16; HL; NHLBI Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/27 (Item 9 from file: 155) DIALOG(R) File 155: MEDLINE(R) PMID: 1854947 06998847 91308625 The effect of leukotriene LTC4 on the coronary vascular bed and on myocardial contractile function] leikotriena Vliianie LTC4 na koronarnoe sosudistoe ruslo i sokratitel'nuiu funktsiiu miokarda. Moibenko A A; Kolchin Iu N; Bulakh V N; Sorochinskii A E Biulleten' eksperimental'noi biologii i meditsiny (USSR) Feb 1991, 111 (2) p120-3, ISSN 0365-9615 Journal Code: 0370627 Document type: Journal Article ; English Abstract Languages: RUSSIAN Main Citation Owner: NLM Record type: Completed

7/3/28 (Item 10 from file: 155) DIALOG(R)File 155:MEDLINE(R)

06955207 91268171 PMID: 1675639 Intracarotid infusion of leukotriene C4 selectively increases blood-brain barrier permeability after focal ischemia in rats. Baba T; Black K L; Ikezaki K; Chen K N; Becker D P Division of Neurosurgery, UCLA Medical Center 90024. Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism (UNITED STATES) Jul 1991, 11 (4) p638-43, ISSN 0271-678X Contract/Grant No.: 1R29NS26523-01; NS; NINDS Journal Code: 8112566 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/29 (Item 11 from file: 155) DIALOG(R) File 155: MEDLINE(R) PMID: 2912339 06028055 89104042 Effect of inhaled leukotriene C4 on cardiopulmonary function. Albazzaz M K; Patel K R; Shakir S; Dargie H J; Reid J M Department of Respiratory Medicine, Western Infirmary, Glasgow, Scotland. American review of respiratory disease (UNITED STATES) Jan 1989, 139 (1) p188-93, ISSN 0003-0805 Journal Code: 0370523 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 12 from file: 155) 7/3/30 DIALOG(R) File 155:MEDLINE(R) 05525066 87274028 PMID: 3608129 Leukotriene C4- and D4-induced diffuse peripheral constriction of swine coronary artery accompanied by ST elevation on the electrocardiogram: angiographic analysis. Tomoike H; Egashira K; Yamada A; Hayashi Y; Nakamura M Circulation (UNITED STATES) Aug 1987, 76 (2) p480-7, ISSN 0009-7322 Journal Code: 0147763 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed (Item 13 from file: 155) 7/3/31 DIALOG(R) File 155: MEDLINE(R) 05503541 87254226 PMID: 3110422 Calcium paradox-evoked release of prostacyclin and immunoreactive leukotriene C4 from rat and guinea-pig hearts. Evidence that endogenous prostaglandins inhibit leukotriene biosynthesis. Karmazyn M Journal of molecular and cellular cardiology (ENGLAND) Mar 1987, 19 (3) p221-30, ISSN 0022-2828 Journal Code: 0262322 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed

7/3/32 (Item 14 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

05340426 87092594 PMID: 3025894 Immunological challenge with virus initiates leukotriene C4 production in the heart and induces cardiomyolysis in guinea pigs. Moshonov S; Ashkenazy Y; Meshorer A; Hurwitz N; Kauli N; Zor U Prostaglandins, leukotrienes, and medicine (SCOTLAND) Nov 1986, 25 (1) p17-26, ISSN 0262-1746 Journal Code: 8206868 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 7/3/33 (Item 15 from file: 155) DIALOG(R) File 155:MEDLINE(R) 05160495 86233587 PMID: 3459198 Cardiovascular effects of leukotriene C4 and D4 in the anesthetized and conscious domestic hen. Wechsung E; Houvenaghel A Prostaglandins, leukotrienes, and medicine (SCOTLAND) Apr 1986, 22 p79-87, ISSN 0262-1746 Journal Code: 8206868 (1) Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed ? t s7/7/27/7/2 (Item 2 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 000093025431 07946333 INTRACORONARY C5A INDUCES MYOCARDIAL ISCHEMIA BY MECHANISMS INDEPENDENT OF THE NEUTROPHIL LEUKOCYTE FILTERS DESENSITIZE THE MYOCARDIUM TO C-5A AUTHOR: ENGLER R L; ROTH D M; DEL BALZO U; ITO B R AUTHOR ADDRESS: RES. SERV., VETERANS ADM. MED. CENT., 3350 LA JOLLA VILLAGE DR., SAN DIEGO, CALIF. 92161, USA. JOURNAL: FASEB (FED AM SOC EXP BIOL) J 5 (14). 1991. 2983-2991. 1991 FULL JOURNAL NAME: FASEB (Federation of American Societies for Experimental Biology) Journal CODEN: FAJOE RECORD TYPE: Abstract LANGUAGE: ENGLISH ABSTRACT: Activation of the complement cascade with the generation of anaphylatoxins accompanies the inflammatory response elicited by acute myocardial ischemia and reperfusion. Although complement is activated in the interstitium during acute myocardial ischemia, we have studied mechanisms whereby complement might exacerbate ischemia by using a model employing intracoronary injection of C5a in nonischemic hearts. Intracoronary injection of complement component C5a induces transient myocardial ischemia, mediated through the production of the coronary vasoconstrictors thromboxane A2 and peptidoleukotrienes (LTC4, LTD4), and causes sequestration of polymorphonuclear leukocytes (PMN) in

the coronary vascular bed. To further investigate the role of the PMN in the C5a-induced vasoconstriction, the left anterior descending coronary artery (LAD) in pigs was perfused at constant pressure and measurements of coronary blood flow, **myocardial** contractile function (sonomicrometry), arterial/coronary venous blood PMN count, and thromboxane B2 (TxB2) levels were performed. The **myocardial**

response to intracoronary C5a (500 ng) was determined before, during and after perfusion with blood depleted of PMNs using leukocyte filters (Sepacell R-500, Pall PL-100). In additional animals, the myocardial response to the PMN chemotactic agent, LTB4, and the effects of intracoronary C5a during constant flow perfusion were measured. Control intracoronary injection of C5a decreased flow (41% of baseline) and contractile function (39% of baseline), PMNs were trapped (5.1 .times. 103 cells/.mu.l), and TxB2 concentration increased in coronary venous blood. The response to C5a during coronary perfusion with arterial blood depleted of PMNs with Sepacell or Pall filters (< 0.1 .times. 103 cells/.mu.l) was greatly blunted, with flow and contractile function falling by less than 14 and 8%, respectively, from baseline, and release of TxB2 was greatly attenuated. However, the myocardial ischemia and TxB2 release remained depressed in response to C5a after removal of the filters and perfusion with either arterial blood containing normal levels of PMNs or stored arterial blood never exposed to filters. In contrast, the repeat C5a challenge resulted in equivalent myocardial extraction of PMNs, thus indicating a dissociation of PMN sequestration from the acute ischemic response and release of TxB2. In a separate experiments, the intracoronary injection of LTB4 also resulted in a pronounced myocardial extraction of PMNs (8.6 .times. 103 cells/.mu.l) greater than during C5a, but did not depress coronary flow or function. Perfusion at constant flow greatly diminished the ischemic response to C5a, indicating that vasoconstriction and resultant ischemia is the main cause of the contractile dysfunction. These data indicate that leukocyte filters inhibit the myocardial ischemia and release of TxB2 induced by C5a via mechanisms not related to PMN depletion. These filters may directly desensitize the myocardium or may induce the release of factors that interfere with the effects of C5a in our model. These data argue against a causal role of microvascular obstruction of PMN trapping in the acute myocardial ischemic response to intravascular activated complement C5a and suggest that the acute ischemic response may have PMN-independent components. However, the longterm contribution to injury of PMNs trapped by complement activation during ischemia requires further study. ? t s7/kwic/2

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7/KWIC/2 (Item 2 from file: 5) DIALOG(R)File 5:(c) 2002 BIOSIS. All rts. reserv.

INTRACORONARY C5A INDUCES **MYOCARDIAL ISCHEMIA** BY MECHANISMS INDEPENDENT OF THE NEUTROPHIL LEUKOCYTE FILTERS DESENSITIZE THE MYOCARDIUM TO C-5A

...ABSTRACT: the complement cascade with the generation of anaphylatoxins accompanies the inflammatory response elicited by acute **myocardial ischemia** and **reperfusion**. Although complement is activated in the interstitium during acute **myocardial ischemia**, we have studied mechanisms whereby complement might exacerbate **ischemia** by using a model employing intracoronary injection of C5a in nonischemic hearts. Intracoronary injection of complement component C5a induces transient **myocardial ischemia**, mediated through the production of the coronary vasoconstrictors thromboxane A2 and peptidoleukotrienes (LTC4, LTD4), and causes sequestration of polymorphonuclear leukocytes (PMN) in the coronary vascular bed. To further...

...artery (LAD) in pigs was perfused at constant pressure and measurements of coronary blood flow, **myocardial** contractile function (sonomicrometry), arterial/coronary venous blood PMN count, and thromboxane B2 (TxB2) levels were performed. The **myocardial** response to intracoronary C5a (500 ng) was determined before, during and after perfusion with blood...

- ...of PMNs using leukocyte filters (Sepacell R-500, Pall PL-100). In additional animals, the **myocardial** response to the PMN chemotactic agent, LTB4, and the effects of intracoronary C5a during constant...
- ...14 and 8%, respectively, from baseline, and release of TxB2 was greatly attenuated. However, the **myocardial ischemia** and TxB2 release remained depressed in response to C5a after removal of the filters and...
- ...arterial blood never exposed to filters. In contrast, the repeat C5a challenge resulted in equivalent **myocardial** extraction of PMNs, thus indicating a dissociation of PMN sequestration from the acute **ischemic** response and release of TxB2. In a separate experiments, the intracoronary injection of LTB4 also resulted in a pronounced **myocardial** extraction of PMNs (8.6 .times. 103 cells/.mu.l) greater than during C5a, but did not depress coronary flow or function. Perfusion at constant flow greatly diminished the **ischemic** response to C5a, indicating that vasoconstriction and resultant **ischemia** is the main cause of the contractile dysfunction. These data indicate that leukocyte filters inhibit the **myocardial ischemia** and release of TxB2 induced by C5a via mechanisms not related to PMN depletion. These...
- ...data argue against a causal role of microvascular obstruction of PMN trapping in the acute **myocardial ischemic** response to intravascular activated complement C5a and suggest that the acute **ischemic** response may have PMN-independent components. However, the longterm contribution to injury of PMNs trapped by complement activation during **ischemia** requires further study.

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File: PGPB

Nov 14, 2002

DOCUMENT-IDENTIFIER: US 20020168366 A1 TITLE: Compositions and methods for producing vascular occlusion

Summary of Invention Paragraph (68):

[0062] As noted above, a composition or method of the present invention includes a platelet specific agent or component. Exemplary platelet specific agents or components include but are not limited to von Willebrand factor (VWF), osteopontin, fibrinogen, fibrin, fibronectin, vitronectin, collagen, thrombospondin, laminin, heparin, heparan sulfate, chondroitin sulfate, phospholipase A2, matrix metalloproteinases (MMPs), thrombin, glass, sialyl-lewis X, fibulin-1, platelet-endothelial cell adhesion molecule (PECAM), intercellular adhesion molecule 1 (ICAM-1), ICAM-2, MAC-1, LFA-1, PSGL-1, either singly or in combination.

Summary of Invention Paragraph (71):

[0065] As noted above, a composition or method of the present invention may include a platelet-mediated occlusion retarder or the like. The platelet-mediated occlusion retarder may be a moiety that forms a portion of a bi-functional molecule as noted above, may be an ingredient in a composition according to the invention, and/or may be administered separately from a composition according to the invention. Those skilled iin the art will recognize that it may be desirable to include or use a platelet-mediated occlusion retarder when the individual receiving therapy based on the method of the present invention has an underlying propensity to thrombose (i.e. form clots too rapidly and/or in inappropriate locations in the body). Although the method of the present invention is directed to the formation of a thrombus in the tumor vasculature, individuals with a propensity to thrombose may form thrombi in inappropriate locations during the course of the therapy described by the present invention. Use of agents to reduce the rapidity and/or extent of thrombosis could be used to minimize the risk of forming thrombi in inappropriate locations in the body. Examples of conditions whereby the individual receiving therapy encompassed by the present invention may require the use of occlusion retarders are, but are not limited to, coronary artery disease, acute myocardial infarction, transient ischemic attack, stroke, high blood pressure, ATIII deficiency, Protein C deficiency, Protein S deficiency, heparin-induced thrombocytopenia, deep vein thrombosis, peripheral vascular disease and/or Factor V Leiden deficiency.

Summary of Invention Paragraph (85):

[0079] Exemplary conditions that may warrant using controllers, retarders, or agents that diminish a method or composition of the invention include but are not limited to pro-thrombotic or pro-coagulant conditions, such as Factor V.sup.Leiden deficiency, antiphospholipid syndrome (APS), Protein C and/or Protein S and/or Antithrombin III deficiency, <u>deep vein</u> thrombosis (DVT), pseudo-von Willebrands disease, Type IIb von Willebrands disease, peripheral vascular disease (PVD), and high blood pressure, among others. Exemplary conditions that may warrant using enhancers or agents that augment a method or composition of the invention include but are not limited to any condition that includes a risk of hemorrhage, including but not limited to coagulation factor deficiencies, hemophilia, thrombocytopenia, and anticoagulation therapy, among others. Also, controlling thrombus generation includes at least one of altering the temperature at the pre-determined site, altering the rate of blood flow at the pre-determined site, and altering the blood pressure at the pre-determined site. WEST

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Nov 29, 2001

DOCUMENT-IDENTIFIER: US 20010046970 A1 TITLE: Inhibition of selectin binding

Summary of Invention Paragraph (20):

[0018] Each of the selectins has a different family of natural ligands on the surface of the opposing cell (see McEver et al., 270:11025, 1995). E-selectin binds strongly to a ligand designated ESL-1. In contrast, antibody blocking studies indicate that essentially all the binding sites for P-selectin on leukocytes are attributable to an O-glycosylated protein designated <u>PSGL-1</u> (P-selectin glycoprotein ligand 1) (Moore et al., J. Cell Biol. 128:661, 1995). The natural ligands identified for L-selectin is neither of these, but include other glycoproteins with the designations GlyCAM-1, CD34, and MAdCAM-1.

Summary of Invention Paragraph (21):

[0019] The binding specificity indicates that at least two of the three selectins must be recognizing a ligand component beyond the sLe.sup.x structure. In addition to the oligosaccharide, P-selectin must bind a site on <u>PSGL-1</u> with features different from ESL-1 and from other mucin-like O-glycosylated proteins, such as CD43.

Summary of Invention Paragraph (24):

[0022] The sulfate component has been mapped more precisely in the structure of the P-selectin ligand <u>PSGL-1</u>. The requirement in P-selectin is provided by one or more sulfated tyrosines near the N-terminus of the polypeptide backbone, separate from the glycosylation site.

Summary of Invention Paragraph (25):

[0023] Wilkins et al. (J. Biol. Chem. 270:22677, 1995) demonstrated that <u>PSGL-1</u> synthesized in human HL-60 cells can be metabolically labeled with [.sup.35S]sulfate. It was shown that most of the .sup.35S label was incorporated into the polypeptide in the form of tyrosine sulfate. Treatment of <u>PSGL-1</u> with a bacterial arylsulfatase released sulfate from tyrosine, and resulted in a concordant decrease in binding to P-selectin.

Summary of Invention Paragraph (26):

[0024] Pouyani et al. (Cell 83:333, 1995) demonstrated that selective inhibitors of sulfation compromised binding of HL-60 cells to soluble P-selectin but not E-selectin. The cell-surface expression of sLe.sup.x or the polypeptide were not compromised by treatment. Deletion analysis of isolated <u>PSGL-1</u> constructs localized the binding component to residues 20-40. The segment contains three tyrosine residues, and when these were changed to phenylalanine, P-selectin binding activity was abolished. Furthermore, when the 20 amino acid segment was fused on to a different protein, it was again sulfated during biosynthesis and had binding activity for P-selectin. These authors suggested that the sulfated tyrosines interact with P-selectin not through the carbohydrate binding domain of P-selectin, but through the EGF-like domain, which is located closer in the protein sequence to the membrane spanning domain.

Summary of Invention Paragraph (27):

[0025] Sako et al. (Cell 83:323, 1995) performed another series of binding experiments using the extracellular domain of <u>PSGL-1</u> expressed as a fusion protein. The assay required fucosylation of the protein and cations in the assay medium, consistent with a dependence on carbohydrates like sLe.sup.x. Mutation of the

putative N-linked glycosylation sites had no effect on selectin binding, suggesting that the carbohydrate requirement was O-linked. However, mutation of three tyrosines to phenylalanine abrogated binding activity for P-selectin. Binding of E-selectin, for which <u>PSGL-1</u> can also act as a ligand, was not affected by removal of the sulfation sites.

Summary of Invention Paragraph (28):

[0026] The binding affinity of P- and L-selectin for sLe.sup.x is in the mM range (Nelson et al., J. Clin Invest. 91:1157,1993). In contrast, the affinity of P-selectin for the natural ligand is in the nM range (Moore et al., J. Cell Biol. 112:491, 1991), a difference in potency of .about.10.sup.6 fold. Synthetic oligosaccharides containing multiple sLe.sup.x units only partly make up the difference, so the effect is not just due to ligand valency. The disparity is also attributable to the requirement of P- and L-selectin for a strong anionic determinant, like the sulfotyrosines on <u>PSGL-1</u>. Compounds effective in the same concentration range as <u>PSGL-1</u> must be able to supply a similarly effective determinant combination.

Summary of Invention Paragraph (39):

[0036] Also embodied are compositions for treating a disease characterized by local alteration in the adherence of leukocytes or cancer cells to vascular endothelium, platelets or lymphatic tissue, comprising a polymerized lipid composition comprising a sheet of lipids wherein a proportion of the lipids are covalently crosslinked, a proportion of the lipids have an attached saccharide, and a proportion of the lipids not having an attached saccharide have an acid group that is negatively charged at neutral pH. Diseases of interest include but are not limited to cardiac disease (such as ischemia reperfusion injury, myocardial infarction, myocarditis, restenosis, and <u>deep vein</u> thrombosis), hemmorhagic shock, arthritis, asthma, and metastatic cancer.

Brief Description of Drawings Paragraph (3):

[0039] FIGS. 2A and 2B depict some of the aspects of selectin binding. In FIG. 2A the boxed panel shows the receptor ligand pairs known for L-, P- and E-selectin. They are depicted on the same cell for convenience, but participate in different ways to cell adhesion and migration. FIG. 2B is a detail showing the dual binding site model for P-selectin. In the ligand <u>PSGL-1</u>, the negative groups correspond to three sulfotyrosine residues. In contrast, there is no evidence for a separate anion binding site for E-selectin.

Detail Description Paragraph (6):

[0050] 3. A negatively charged or electronegative group (usually a carboxylic acid or oxyacid) that meets the anionic binding requirement of P- and L-selectin. There is no requirement that the group play exactly the same role as the sulfotyrosines of PSGL-1, as long as the anionic binding requirement is satisfied.

Detail Description Paragraph (9):

[0053] The negatively charged group of the natural ligand <u>PSGL-1</u> is sulfotyrosine, and the nature of what would be required to satisfy the anionic binding requirement in liposomes was unknown. It was found that the anionic binding requirement does not require the anion to be on a protein or carbohydrate component, but can be directly coupled to lipids that become part of the lipid sheet. Surprisingly, the anionic component need not be a sulfate group, but can be provided as a simple carboxylic acid headgroup on the lipid.

Detail Description Paragraph (59):

[0103] Polymerized liposomes of this invention can be classified on the basis of their potency in various test assays known in the art. For example, when tested for inhibition of the binding of isolated selectin to cells expressing a selectin ligand such as <u>PSGL-1</u>, the liposomes preferably are able to inhibit the binding in a manner that attains 50% maximal inhibition (IC.sub.50) at a concentration of no more than about 10 TM, preferably no more than about 1 TM, still more preferably no more than about 100 nM, and even more preferably no more than about 10 nM oligosaccharide equivalents. A preferred binding assay of this type uses HL-60 cells, and is illustrated in Example 2. Polymerized liposomes may also be categorized in any assay on the basis of the relative IC.sub.50 compared with a suitable standard. The standard may be an oligosaccharide presented uncomplexed to liposomes or in a monomeric form, such as sLe.sup.x or sLe.sup.x analog. The standard may also be a liposome having no oligosaccharide but otherwise the same lipid composition, or a liposome made with 100% carboxy terminated or hydroxy terminated lipids. In certain embodiments, the polymerized liposomes have an IC.sub.50 which is preferably 10.sup.2-fold lower, more preferably about 10.sup.3-fold lower, more preferably about 10.sup.4-fold lower, still more preferably about 10.sup.5-fold lower, and even more preferably about 10.sup.6-fold lower than that of the standard.

Detail Description Paragraph (72):

[0116] A convenient one-cell assay for P-selectin inhibitors makes use of HL-60 cells, available from the ATCC. HL-60 cells naturally express the <u>PSGL-1</u> antigen at about 36,000 sites per cell (Ushiyama et al., J. Biol. Chem. 268:15229, 1993). The assay is described in Brandley et al. (Glycobiol. 3:633, 1993). Briefly, an E or P-selectin chimera is incubated with biotinylated goat F(ab'), anti-human IgG Fc, and an alkaline phosphatase-streptavidin conjugate for 30 min. This complex is then incubated with potential inhibitors for .about.45 min at 37.degree. C. 50 TL of the mixture is added to each well of round-bottom microtiter plates previously blocked with BSA. An equal volume of an HL-60 cell suspension is added and the plate is incubated for 45 min at 4.degree. C. Cells are pelleted to the well bottoms by centrifugation, washed, and developing using p-nitrophenyl phosphate.

Detail Description Paragraph (90):

[0134] Reperfusion injury is a major problem in clinical cardiology. Therapeutic agents that reduce leukocyte adherence in ischemic myocardium can significantly enhance the therapeutic efficacy of thrombolytic agents. Thrombolytic therapy with agents such as tissue plasminogen activator or streptokinase can relieve coronary artery obstruction in many patients with severe myocardial ischemia prior to irreversible myocardial cell death. However, many such patients still suffer myocardial necrosis despite restoration of blood flow. Reperfusion injury is known to be associated with adherence of leukocytes to vascular endothelium in the ischemic zone, presumably in part because of activation of platelets and endothelium by thrombin and cytokines that makes them adhesive for leukocytes (Romson et al., Circulation 67:1016, 1983). The adherent leukocytes can migrate through the endothelium and destroy ischemic myocardium just as it is being rescued by restoration of blood flow. Ischemia may occur pursuant to a myocardial infarction or as a result of complications of surgery, such as <u>deep vein</u> thrombosis. Another inflammatory condition of concern in cardiology is restenosis.

Detail Description Paragraph (155):

[0194] Glycoliposomes containing 5% sulfo Le.sup.x analog and 95% hydroxyl-terminated lipid were tested in a flow adhesion assay (Alon et al., Nature 374:539, 1995). Briefly, P-selectin chimera is immobilized in a flow chamber and the affinity of HL-60 cells for this substrate is manifest for their ability to roll slowly along on the surface. The interaction is specific for the <u>PSGL-1</u> mucin domain on the HL-60 cells and the inhibitor's ability to block cell adhesion under physiological flow rather than under static conditions. At a glycolipid concentration of 1 TM, this glycoliposome formulation was able to completely inhibit HL-60 cell rolling on P-selectin surfaces. The control liposome (without the carbohydrate) had no effect.

Detail Description Paragraph (172):

[0209] Treated animals in the cited studies responded to 400 Tg/kg of sLe.sup.x presented as a phospholipid liposome, or 1 mg/kg of the anti-L-selectin monoclonal antibody DREG-200. In the present experiment, polymerized liposomes are tested in a range of about 10-400 Tg of carbohydrate equivalent per kg body weight. An equal number of polymerized liposomes made of 100% neutral lipids is given at an equal dose (on a per-liposome basis) as vehicle control. To the extent that necrosis induced by other types of acute cardiac inflammatory events, such as myocarditis, restenosis and deep vein thrombosis, are mediated by similar mechanisms, the effective doses established in the cardiac reperfusion model may also be considered for these conditions.

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12282749 BIOSIS NO.: 20000036251
Effect of recombinant PSGL-1 (rPSGL-Ig) on vascular injury and
  thrombosis following venous stasis.
AUTHOR: Eppihimer Michael J(a); Schaub Robert G(a
AUTHOR ADDRESS: (a)Genetics Inst, Inc, Andover, MA**USA
JOURNAL: Circulation 110 (18 SUPPL.):pI812 Nov. 2, 1999
CONFERENCE/MEETING: 72nd Scientific Sessions of the American Heart
Association Atlanta, Georgia, USA November 7-10, 1999
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5838989 TREAT? 1866221 PREVENT? 5412093 THERAP? 232406 . . . 33 PSGL? AND (THROMBOSIS OR THROMBOTIC OR RESTENSOSIS OR S4 STENOSIS OR REPEFUSION OR ISCHEM?) (20N) (INHIBIT? OR SUPPRESS? OR TREAT? OR PREVENT? OR THERAP?) ? rd s4 ... completed examining records 23 RD S4 (unique items) S5 ? t s5/3/all (Item 1 from file: 5) 5/3/1 DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 13632735 BIOSIS NO.: 200200261556 In vivo real time imaging of arterial thrombus formation reveals P-selectin- and PSGL-1-mediated tissue factor accumulation as a mechanism for fibrin clot generation. AUTHOR: Falati Shahrokh(a); Gross Peter(a); Merrill-Skoloff Glenn(a); Croce Kevin(a); Furie Barbara C(a); Furie Bruce(a) AUTHOR ADDRESS: (a)Center for Hemostasis and Thrombosis Research, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA** USA JOURNAL: Blood 98 (11 Part 1):p823a November 16, 2001 MEDIUM: print CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971 RECORD TYPE: Abstract LANGUAGE: English 5/3/2 (Item 2 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 13205270 BIOSIS NO.: 200100412419 Prevention of intimal hyperplasia with recombinant soluble P-selectin glycoprotein ligand-immunoglobulin in the porcine coronary artery balloon injury model. AUTHOR: Wang Kai; Zhou Zhongmin; Zhou Xiaorong; Tarakji Khaldoun; Topol Eric J; Lincoff A Michael(a) AUTHOR ADDRESS: (a)Cardiology Department, Cleveland Clinic Foundation, 9500 Euclid Ave., F25, Cleveland, OH, 44195: lincofa@ccf.org**USA JOURNAL: Journal of the American College of Cardiology 38 (2):p577-582 August, 2001 MEDIUM: print ISSN: 0735-1097 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English SUMMARY LANGUAGE: English 5/3/3 (Item 3 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 13199175 BIOSIS NO.: 200100406324 P-selectin antagonism with recombinant P-selectin glycoprotein ligand-1 (rPSGL-Ig) inhibits circulating activated platelet binding to neutrophils induced by damaged arterial surfaces.

AUTHOR: Theoret Jean-Francois; Bienvenu Jean-Guy; Kumar Anjali; Merhi Yahye (a) AUTHOR ADDRESS: (a)Research Center, Montreal Heart Institute, 5000 Belanger Street East, Montreal, PQ, H1T 1C8: merhi@icm.umontreal.ca**Canada JOURNAL: Journal of Pharmacology and Experimental Therapeutics 298 (2):p 658-664 August, 2001 MEDIUM: print ISSN: 0022-3565 DOCUMENT TYPE: Article **RECORD TYPE: Abstract** LANGUAGE: English SUMMARY LANGUAGE: English 5/3/4 (Item 4 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. BIOSIS NO.: 200100320681 13113532 Polymorphisms of P-selectin glycoprotein ligand-1 (PSGL-1) are associated with neutrophil-platelet adhesion and with ischemic cerebrovascular disease. AUTHOR: Lozano M L(a); Gonzalez-Conejero R(a); Corral J(a); Rivera J(a); Iniesta J A(a); Martinez C(a); Vicente V(a) AUTHOR ADDRESS: (a)Units of Hematology/Clinical Oncology and Neurology, University General Hospital, Murcia**Spain JOURNAL: Blood 96 (11 Part 1):p643a November 16, 2000 MEDIUM: print CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 SPONSOR: American Society of Hematology ISSN: 0006-4971 RECORD TYPE: Abstract LANGUAGE: English SUMMARY LANGUAGE: English 5/3/5 (Item 5 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 12861763 BIOSIS NO.: 200100068912 Myocardial protection by recombinant soluble P-selectin glycoprotein ligand-1: Suppression of neutrophil and platelet interaction following ischemia and reperfusion. AUTHOR: Ham Sang Soo; Jang Yoon Young; Song Jin Ho; Lee Hyang Mi; Kim Kwang Joon; Hong Jun Sik; Shin Yong Kyoo(a) AUTHOR ADDRESS: (a) Department of Pharmacology, College of Medicine, Chung-Ang University, Seoul, 156-756: yks@cau.ac.kr**South Korea JOURNAL: Korean Journal of Physiology & Pharmacology 4 (6):p515-523 December, 2000 MEDIUM: print ISSN: 1226-4512 DOCUMENT TYPE: Article **RECORD TYPE:** Abstract LANGUAGE: English SUMMARY LANGUAGE: English 5/3/6 (Item 6 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 11937821 BIOSIS NO.: 199900183930

Recombinant soluble form of **PSGL**-1 accelerates thrombolysis and prevents reocclusion in a porcine model. AUTHOR: Kumar Anjali(a); Villani Mario P; Patel Umesh K; Keith James C Jr ; Schaub Robert G AUTHOR ADDRESS: (a)Preclinical R and D, Genetics Institute, Inc., One Burtt Rd, Andover, MA, 01810**USA JOURNAL: Circulation 99 (10):p1363-1369 March 16, 1999 ISSN: 0009-7322 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English 5/3/7 (Item 7 from file: 5) DIALOG(R)File 5:Biosis Previews(R) (c) 2002 BIOSIS. All rts. reserv. 11876919 BIOSIS NO.: 199900123028 Recombinant soluble P-selectin glycoprotein ligand-1 protects against myocardial ischemic reperfusion injury in cats. AUTHOR: Hayward Reid; Campbell Barry; Shin Yong K; Scalia Rosario; Lefer Allan M(a) AUTHOR ADDRESS: (a)Dep. Physiol., Jefferson Med. Coll., Thomas Jefferson Univ., Philadelphia, PA 19107**USA JOURNAL: Cardiovascular Research 41 (1):p65-76 Jan., 1999 ISSN: 0008-6363 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English (Item 1 from file: 73) 5/3/8 DIALOG(R)File 73:EMBASE (c) 2002 Elsevier Science B.V. All rts. reserv. EMBASE No: 2002432787 11860822 KF38789: Treatment of ischemia reperfusion injury P-selectin inhibitor Miki I.; Ohta S.; Inujima Y.; Abe M.; Uosaki Y.; Saro S. I. Miki, Biomedical Research Laboratories, Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Shimotogari 1188, Sunto, Shizuoka 411-8731 Japan Drugs of the Future (DRUGS FUTURE) (Spain) 01 SEP 2002, 27/9 (837 - 840)CODEN: DRFUD ISSN: 0377-8282 DOCUMENT TYPE: Journal ; Article LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH NUMBER OF REFERENCES: 23 5/3/9 (Item 2 from file: 73) DIALOG(R)File 73:EMBASE (c) 2002 Elsevier Science B.V. All rts. reserv. 11534443 EMBASE No: 2002106102 P-selectin and **PSGL**-1: Exploiting connections between inflammation and venous thrombosis McEver R.P. Dr. R.P. McEver, Warren Medical Research Institute, University of Oklahoma, Health Sciences Center, 825 N.E. 13th Street, Oklahoma City, OK 73104 United States AUTHOR EMAIL: rodger-mcever@ouhsc.edu Thrombosis and Haemostasis (THROMB. HAEMOST.) (Germany) 2002, 87/3 (364 - 365)

CODEN: THHAD ISSN: 0340-6245 DOCUMENT TYPE: Journal ; Note LANGUAGE: ENGLISH NUMBER OF REFERENCES: 27 (Item 3 from file: 73) 5/3/10 DIALOG(R)File 73:EMBASE (c) 2002 Elsevier Science B.V. All rts. reserv. EMBASE No: 2001030587 11010507 Myocardial protection by recombinant soluble P-selectin glycoprotein ligand-1: Suppression of neutrophil and platelet interaction following ischemia and reperfusion Sang Soo Ham; Yoon Young Jang; Jin Ho Song; Hyang Mi Lee; Kwang Joon Kim; Jun Sik Hong; Yong Kyoo Shin Y.K. Shin, Department of Pharmacology, College of Medicine, Chung-Ang University, Seoul 156-756 South Korea AUTHOR EMAIL: yks@cau.ac.kr Korean Journal of Physiology and Pharmacology (KOREAN J. PHYSIOL. PHARMACOL.) (South Korea) 2000, 4/6 (515-523) CODEN: KJPPF ISSN: 1226-4512 DOCUMENT TYPE: Journal ; Article LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH NUMBER OF REFERENCES: 30 5/3/11 (Item 4 from file: 73) DIALOG(R)File 73:EMBASE (c) 2002 Elsevier Science B.V. All rts. reserv. 07598941 EMBASE No: 1999092826 Reduction of hepatic ischemia/reperfusion injury by a soluble P-selectin glycoprotein ligand-1 Dulkanchainun T.S.; Goss J.A.; Imagawa D.K.; Shaw G.D.; Anselmo D.M.; Kaldas F.; Wang T.; Zhao D.; Busuttil A.A.; Kato H.; Murray N.G.B.; Kupiec-Weglinski J.W.; Busuttil R.W.; Meyers W.C.; Klintmalm G.; Diethelm A.G. Dr. R.W. Busuttil, Div. of Liver/Pancreas Transplant., UCLA School of Medicine, CHS 77-120, 10833 Le Conte Ave., Los Angeles, CA 90095 United States Annals of Surgery (ANN. SURG.) (United States) 1998, 227/6 (832-840) CODEN: ANSUA ISSN: 0003-4932 DOCUMENT TYPE: Journal; Article LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH NUMBER OF REFERENCES: 42 5/3/12 (Item 1 from file: 155) DIALOG(R) File 155: MEDLINE(R) PMID: 11861775 12983553 21851020 Role of inflammatory mediators in thrombogenesis. Shebuski Ronald J; Kilgore Kenneth S CarePoint Diagnostics, Inc., Eden Prairie, Minnesota 55344, USA. CVR2000@portup.com Journal of pharmacology and experimental therapeutics (United States) Mar 2002, 300 (3) p729-35, ISSN 0022-3565 Journal Code: 0376362 Document type: Journal Article; Review; Review, Tutorial Languages: ENGLISH Main Citation Owner: NLM Record type: Completed

(Item 2 from file: 155) 5/3/13 DIALOG(R) File 155: MEDLINE(R) 21198708 PMID: 11303727 11176227 Evaluation of the safety of recombinant P-selectin glycoprotein ligand-immunoglobulin G fusion protein in experimental models of localized and systemic infection. Opal S M; Sypek J P; Keith J C; Schaub R G; Palardy J E; Parejo N A Infectious Disease Division, Brown University School of Medicine, Providence, Rhode Island, USA. Shock (Augusta, Ga.) (United States) Apr 2001, 15 (4) p285-90, ISSN 1073-2322 Journal Code: 9421564 Document type: Journal Article Languages: ENGLISH Main Citation Owner: NLM Record type: Completed 5/3/14 (Item 1 from file: 399) DIALOG(R)File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 137336464 CA: 137(23)336464w JOURNAL Thrombolytic P-selectin inhibitor rPSGL-Ig in treatment of acute myocardial infarction AUTHOR(S): Diaz-Ricart, Maribel; Bozzo, J. LOCATION: Servicio de Hemoterapia y Hemostasia, Hospital Clinic, Barcelona, Spain, 08036 JOURNAL: Drugs Future (Drugs of the Future) DATE: 2002 VOLUME: 27 NUMBER: 4 PAGES: 346-349 CODEN: DRFUD4 ISSN: 0377-8282 LANGUAGE: English PUBLISHER: Prous Science (Item 2 from file: 399) 5/3/15 DIALOG(R)File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 137184110 CA: 137(13)184110n JOURNAL New and effective treatment of experimentally induced venous thrombosis with anti-inflammatory rPSGL-Ig AUTHOR(S): Myers, Daniel; Wrobleski, Shirley; Londy, Frank; Fex, Beverly; Hawley, Angela; Schaub, Robert; Greenfield, Lazar; Wakefield, Thomas LOCATION: The Unit for Laboratory Animal Medicine, University of Michigan Ann Arbor, MI, USA JOURNAL: Thromb. Haemostasis (Thrombosis and Haemostasis) DATE: 2002 VOLUME: 87 NUMBER: 3 PAGES: 374-382 CODEN: THHADO ISSN: 0340-6245 LANGUAGE: English PUBLISHER: Schattauer GmbH 5/3/16 (Item 3 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. CA: 137(8)108286j 137108286 PATENT Antibodies and fragments against epitopes present on cancer, metastatic or leukemia cells and platelets for diagnosis and therapy of tumor, metastasis, leukemia, autoimmune disease, and inflammation INVENTOR(AUTHOR): Lazarovits, Janette; Hagai, Yocheved; Plaksin, Daniel; Vogel, Tikva; Nimrod, Abraham; Mar-Haim, Hagit; Szanthon, Ester; Richter, Tamar; Amit, Boaz; Kooperman, Lena; Peretz, Tuvia; Levanon, Avigdor LOCATION: USA ASSIGNEE: Bio-Technology General Corp. PATENT: PCT International ; WO 200253700 A2 DATE: 20020711 APPLICATION: WO 2001US49442 (20011231) *US 751181 (20001229) *US PV258948

(20001229)PAGES: 310 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG 5/3/17 (Item 4 from file: 399) DIALOG(R)File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. CA: 136(16)241673d PATENT 136241673 Inhibition of stenosis or restenosis by p-selectin antagonists, such as PSGL-1 and antibody INVENTOR (AUTHOR) : Kumar, Anjali; Schuab, Robert G.; Tanguay, Jean-Francois; Merhi, Yahye LOCATION: USA ASSIGNEE: Genetics Institute, Inc.; Montreal Heart Institute PATENT: PCT International ; WO 200222820 A1 DATE: 20020321 APPLICATION: WO 2000US25007 (20000912) PAGES: 66 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/12A; C12N-009/64B; C12N-015/62B; C07K-014/705B DESIGNATED COUNTRIES: AE; AG; AL ; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH ; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG 5/3/18 (Item 5 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 136000640 CA: 136(1)640k PATENT Methods for diagnosing and treating hemostatic disorders by modulating P-selectin activity INVENTOR (AUTHOR): Wagner, Denisa D.; Andre, Patrick; Hartwell, Daqing W.; Hrachovinova, Ingrid LOCATION: USA ASSIGNEE: The Center for Blood Research PATENT: PCT International ; WO 200189564 A2 DATE: 20011129 APPLICATION: WO 2001US16021 (20010517) *US PV205734 (20000519) PAGES: 93 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A; A61K-048/00B; A61K-038/17B; A61K-035/14B; A61P-007/00B; A61P-009/00B; A61P-035/00B; G01N-033/50B; G01N-033/86B; G01N-033/68B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

(Item 6 from file: 399) 5/3/19 DIALOG(R)File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 135271307 CA: 135(19)271307j PATENT Inhibition of thrombosis by treatment with P-selectin ligand and P-selectin glycoprotein 1 INVENTOR (AUTHOR): Eppihimer, Michael J.; Schaub, Robert G.; Harris, Alan S LOCATION: USA ASSIGNEE: Genetics Institute, Inc. PATENT: PCT International ; WO 200175107 A2 DATE: 20011011 APPLICATION: WO 2001US10622 (20010402) *US PV193787 (20000331) PAGES: 73 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/12A; C07K-014/47B; C12N-015/62B; A61K-038/17B; A61P-007/02B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG ; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG (Item 7 from file: 399) 5/3/20 DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. CA: 134(22)308960z JOURNAL 134308960 P-selectin-dependent inhibition of thrombosis during venous stasis AUTHOR(S): Eppihimer, Michael J.; Schaub, Robert G. LOCATION: Discovery Research, Immunology, Wyeth/Genetics Institute, Inc., Andover, MA, 01810, USA JOURNAL: Arterioscler., Thromb., Vasc. Biol. DATE: 2000 VOLUME: 20 NUMBER: 11 PAGES: 2483-2488 CODEN: ATVBFA ISSN: 1079-5642 LANGUAGE: English PUBLISHER: Lippincott Williams & Wilkins 5/3/21 (Item 8 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. 128136307 CA: 128(12)136307z JOURNAL Prevention of late renal changes after initial ischemia/reperfusion injury by blocking early selectin binding AUTHOR(S): Takada, Moriatsu; Nadeau, Kari C.; Shaw, Gray D.; Tilney, Nicholas L. LOCATION: Surgical Research Laboratory, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, 02115, USA JOURNAL: Transplantation DATE: 1997 VOLUME: 64 NUMBER: 11 PAGES: 1520-1525 CODEN: TRPLAU ISSN: 0041-1337 LANGUAGE: English PUBLISHER: Williams & Wilkins (Item 9 from file: 399) 5/3/22 DIALOG(R) File 399:CA SEARCH(R) (c) 2002 American Chemical Society. All rts. reserv. CA: 126(21)272038y JOURNAL 126272038 Early cellular and molecular changes in ischemia/reperfusion injury: inhibition by a selectin antagonist, P-selectin glycoprotein ligand-1 AUTHOR(S): Takada, M.; Nadeau, K.C.; Shaw, G.D.; Tilney, N.L. LOCATION: Surgical Research Laboratory, Harvard Medical School and

Department of Surgery, Brigham and Women's Hospital, Boston, MA, 02115, USA JOURNAL: Transplant. Proc. DATE: 1997 VOLUME: 29 NUMBER: 1/2 PAGES: 1324-1325 CODEN: TRPPA8 ISSN: 0041-1345 LANGUAGE: English PUBLISHER: Elsevier

5/3/23 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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126152793 CA: 126(12)152793u PATENT P-selectin ligands and related molecules for treatment of inflammatory and circulatory disorders INVENTOR (AUTHOR): Seed, Brian; Pouyani, Tara LOCATION: USA ASSIGNEE: General Hospital Corporation PATENT: PCT International ; WO 9700079 A1 DATE: 19970103 APPLICATION: WO 96US10043 (19960611) *US 213 (19950614) PAGES: 81 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-038/02A; C07K-014/00B; C07K-014/435B; C07K-014/705B; C12N-015/11B; C12N-015/12B; C12N-015/63B DESIGNATED COUNTRIES: AU; BR; BY; CA; CZ; FI; HU; IL; JP; KR; MX; NO; NZ; RU; SI; TR; UA DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FI ; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE ?

U.S. Patents Fulltext 1980-1989 (File 653) ***Washington Post (File 146) ***Books in Print (File 470) ***Court Filings (File 793) ***Publishers, Distributors & Wholesalers of the U.S. (File 450) ***State Tax Today (File 791) ***Tax Notes Today (File 790) ***Worldwide Tax Daily (File 792) ***New document supplier IMED has been changed to INFOTRIE (see HELP OINFOTRI) >>> Enter BEGIN HOMEBASE for Dialog Announcements <<< >>> of new databases, price changes, etc. <<< * * * * * ** * * File 1:ERIC 1966-2002/Dec 13 (c) format only 2002 The Dialog Corporation Set Items Description ------ - -Cost is in DialUnits ? b 410 22dec02 10:12:09 User208760 Session D2232.1 \$0.34 0.098 DialUnits File1 \$0.34 Estimated cost File1 \$0.34 Estimated cost this search \$0.34 Estimated total session cost 0.098 DialUnits File 410:Chronolog(R) 1981-2002/Nov (c) 2002 The Dialog Corporation Set Items Description --- ---- ------? set hi ;set hi HILIGHT set on as '' HILIGHT set on as '' ? begin 5,73,155,399 22dec02 10:12:14 User208760 Session D2232.2 \$0.00 0.070 DialUnits File410 \$0.00 Estimated cost File410 \$0.01 TELNET \$0.01 Estimated cost this search \$0.35 Estimated total session cost 0.167 DialUnits SYSTEM:OS - DIALOG OneSearch File 5:Biosis Previews(R) 1969-2002/Dec W3 (c) 2002 BIOSIS *File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT. File 73:EMBASE 1974-2002/Dec W3 (c) 2002 Elsevier Science B.V. *File 73: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT. File 155:MEDLINE(R) 1966-2002/Nov W3 *File 155: For updating information please see Help News155. Alert feature enhanced with customized scheduling. See HELP ALERT. File 399:CA SEARCH(R) 1967-2002/UD=13725 (c) 2002 American Chemical Society *File 399: Use is subject to the terms of your user/customer agreement. Alert feature enhanced for multiple files, etc. See HELP ALERT.